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ON THE RELATIONS BETWEEN STOMATITIS PUSTULOSA CONTAGIOSA IN THE HORSE AND POX IN DOMESTIC ANIMALS AND HUMANS

Berliner Tierärztliche Wochenschrift (Berlin Weekly on Veterinary Medicine), Vol. 40, No. 52, 26 December 1924, pp. 757-761.

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(A lecture accompanied with projected slides)
Presented at the 88th meeting of the Association of German Natural Scientists and Physicians (Gesellschaft Deutscher Naturforscher und Ärzte), in Innsbruck.

Stomatitis pustulosa contagiosa is a relatively rarely occurring infectious disease of horses that may be recognized by small nodules of pin-head to pea size at the somewhat reddened and swollen mucous tissue of the mouth. The small nodules develop continuously until they more or less fully cover the mucous tissue of the lips, the corners of the lips, the gum, the cheeks, the tongue, especially the area of the small tongue band and the bottom surface and sides of the tongue. The small nodules rapidly develop into small blisters with a clear, serum-like content. The content of these small blisters becomes turbid after a short period of time, thereby transforming the blister into a pustule. In the small blister or pustula stage, ulcers develop at the blister top after the latter breaks: the base of these blisters deepens and the ulcer consists of slightly bleeding granulation tissue. The ulcers heal relatively fast and leave a whitish scar which, in due course, becomes invisible. The changes in the mucous tissue are accompanied by more or less pronounced swelling of the lips, the cheeks, and the submaxillar lymphal nodes.

The internal body temperature of the afflicted horse is somewhat higher than normal at the beginning and during the pustulo stage; however, it quickly returns to normal at the end of this stage. In other respects, the general attitude of the animals is hardly affected at all. However, the desire to eat is more or less affected, depending on the extent of the prevailing efflorescence; a flow of saliva and a foul mouth-odor is also evident in the course of the disease.

If the process extends to the nasal mucous membrane, nodules and pustules develop at the reddened and swollen nasal mucous membrane on the inner surface of the nasal wing, less often at the sidewall of the nose, and almost always in the vicinity of the boundary of the general cover. This papulous and pustulous inflammation of the nose is accompanied by a slimy-pussy nasal discharge. Less frequently, the conjunctival tissue of the eyes and even the cornea itself are afflicted. In addition, the described changes sometimes develop at the mucous membrane of the anterior cranial auricle and of the vaginal lips. Furthermore, nodules, small blisters, pustules, and ulcers may develop on the skin. The skin areas afflicted may include the lips, the nasal wings, the cheeks, the breast, the forearm, the intestinal area, the anal area, the reproductive organs, the area of the thigh, and especially the fetlock. The number of skin efflorescence varies within very wide limits. In some instances there are only a few single ones, and in some other instances they are scattered over the entire body.

As a rule, the course of the disease is benign; within 10-14 days, in some rare cases after 3-4 weeks, the animal recovers. In exceptional cases, the disease takes an unfavorable, lethal course. Klose reported recently on such a case at the Froehner clinic.

There are divergent views among the doctors of veterinary medicine with respect to the nature of the disease. Whereas French experts held the view since a long time (Marosse, Leblanc, Bouley) that the disease must be considered an equine pox and is the same as the disease called 'grease' and 'sore heels' by Jenner -- the disease that Jenner considers as a successor of cattle pox and found to be transmittable by Loy in 1802 from horse to cattle and thence to the human -- and whereas this disease has no name of its own in France and is simply called as a 'horse pox,' the Germans hold an entirely different view. In Germany, the disease is called 'stomatitis pustulosa contagiosa,' a term originated by Eggeling and Ellenberger, and adopted by Friedberger; it was subsequently extended by Dieckerhoff as 'stomatitis et dermatitis pustulosa contagiosa' since it is not restricted solely to the mucous membranes. Eggeling and Ellenberger gave a very detailed description of the disease in the year of 1878. They also observed spontaneous transfer of the disease to humans. They also succeeded to transfer stomatitis pustulosa artificially to horses, cattle, humans, sheep, and hogs, whereas the susceptibility of goats, rabbits, and dogs remained an unsolved question. Friedberger succeeded in transferring stomatitis to horses, to a cattle, to a sheep, and to a chicken; in the case of the latter, there developed a pox-like rash at the crest.

The strand taken by Eggeling and Ellenberger with respect to the relation between stomatitis pustulosa contagiosa and pox, originates from a remark made by these authors in connection with a publication of Silvani. Silvani described an outbreak of equine pox where the site of the pox was solely in the mouth cavity; this outbreak involved approximately 200 horses. In connection with this report, Eggeling and Ellenberger remarked: "The nodules and pustules observed by us under the microscope cannot be confused with pox." Thus, they definitely rejected the pox-like nature of the disease.

Friedberger recommended the term 'pox affliction' for the disease and stressed that he selected this term to differentiate it from real pox. Dieckerhoff ... [sentence not completed in original source]

De Jong reported in 1918 the results of his experimental investigations on the relations between the disease under discussion and pox in domestic animals and humans. During an outbreak of stomatitis pustulosa contagiosa among army horses in the Netherlands he also definitely rejected a pox-like nature for the disease, by stating that whereas the artificial vaccinability of the variola and the vaccine to horses cannot be denied, there is still nothing known about the pox transmitted to horses by natural infection. He succeeded in transvaccinating the disease onto healthy horses, cattle, rabbits, and humans, whereby the stomatitis material created the same nodules and pustules on the skin as were observed on the mucous membrane of the lip. The infection material employed proved to remain infectious even after passage through Chamberland filters B and F. In addition, de Jong was able to produce the syndrome of stomatitis pustulosa contagiosa in horses by the vaccine obtained from cattle. He also proved that the horse that was afflicted with natural stomatitis pustulosa contagiosa became immune to the vaccine. The same pox eruption could be induced in the calf and the rabbit with stomatitis material and vaccine. Rabbits that were vaccinated with the vaccine showed an early reaction upon revaccination with stomatitis material. Guarnieri particles could be identified in rabbits after transfer of stomatitis virus to the corneal tissue. De Jong further proved that the vaccine obtained from horse through cattle is equally suitable for creating a pox vaccine for humans, and the usual revaccination reaction is shown in humans who were prevaccinated in this manner. The investigations of de Jong culminate in the conclusion that equine stomatitis pustulosa contagiosa is in fact the most frequently occurring form of the Jennerian equine pox.

Van Heelsbergen also initiated studies on the relations between stomatitis pustulosa contagiosa in horses and pox in domestic animals, and between the various pox types in the different domestic animals. He confirmed the findings of de Jong, and considered it likely that the viruses from variola, vaccine, spontaneous cattle pox, stomatitis equi, poultry pox, poultry diphtheria, are variations of the same original virus. Van Heelsbergen successfully transferred the virus of stomatitis pustulosa contagiosa from horses to chicken, and vice versa, using poultry pox material in the latter case. Chicken in which pox developed at the crest following vaccination with stomatitis material, on the other hand, were not immune against subsequent infection

with natural poultry pox. The vaccine virus behaves differently in this connection: it securely protected the poultry against the virus of poultry pox and stomatitis to a certain degree. Van Heelsbergen attributes the strongest immunisatory effectiveness to it among the viruses of the various pox types.

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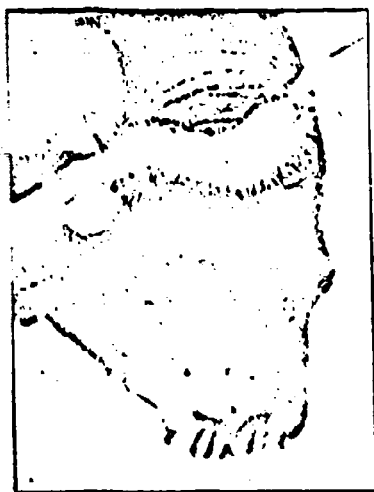


Fig. 1. Stomatitis pustulosa contagiosa in the horse

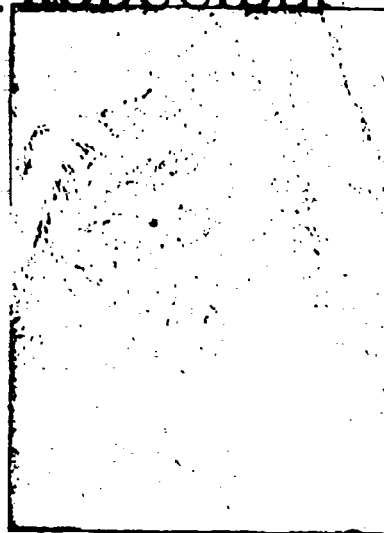


Fig. 2. Pox in a calf after vaccination with stomatitis virus on 24 March 1924. Picture was taken on 29 March 1924.

Toth, who was also active in studies in this field and who instituted numerous transfer tests, concluded that there are near-etiological relations between stomatitis pustulosa contagiosa of the horse and the variola vaccine, whereas cattle and poultry pox are etiologically quite different diseases, and that there is no etiological relation between cattle and sheep pox.

During March of this year, I had an opportunity to perform some tests on a horse that was afflicted with stomatitis pustulosa contagiosa, at the clinic for veterinary medicine. I shall now present a brief report about these tests. The horse showed the usual symptoms of the disease. One could see small, about lentil-sized nodules and pustules, that partly exhibited erosions at the top, at the internal surfaces of the upper and the lower lip, especially at the mucous membrane of the latter. The nodules, pustules, and ulcers were found in especial abundance at the mucous membrane

of the lip corner and the cheek. Furthermore, there were many of them at the sides of the tongue and especially at the small band of the tongue. The general attitude of the horse was not much affected. When admitted, it had a temperature of 39.8°C but the temperature reverted to normal during the next day. The appetite of the animal was slightly less than usual (this was the reason why it was admitted to the clinic). Whereas the horse did drink, it refused to consume hay or grain. It improved rapidly and was discharged from the clinic a few days later in an almost cured condition.

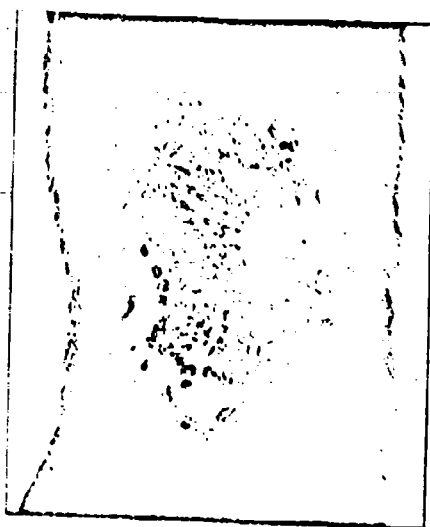


Fig. 3. Pox in the rabbit after vaccination with stomatitis virus on 24 March 1924. Picture was taken on 29 March 1924.

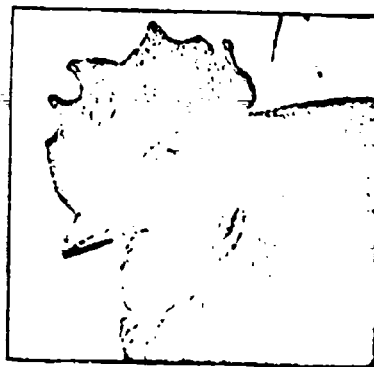


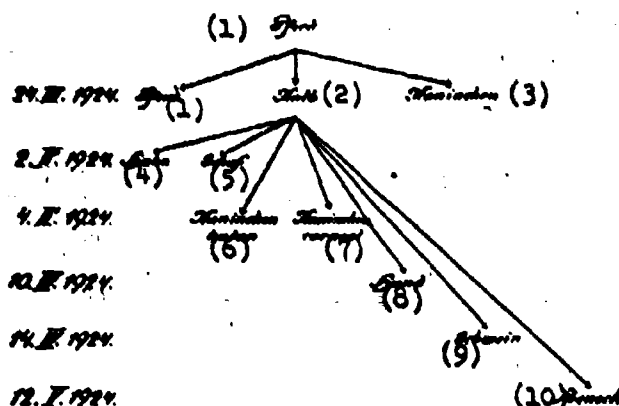
Fig. 4. Pox in the chicken after vaccination with stomatitis virus on 2 April 1924. Picture was taken on 8 April 1924.

The following transfer experiments were conducted with diseased mouth mucous membrane scraped off from this horse:

- 1) onto the mouth mucous membrane of a horse. In this horse, only a very few, but very typical, pustules developed about four days later.
- 2) onto the skin of a calf. Very beautiful papellae and pustules developed in the calf 5-6 days later. They were clearly recognizable as pox on the basis of their general appearance and the central depression.
- 3) the transfer tests with the stomatitis material onto the skin of two rabbits have also shown positive results. The rabbits exhibited the typical picture for vaccination pox.

Additional artificial infections -- involving a sheep, a hog, a dog, two rabbits, a human, and a chicken -- were performed with the stomatitis material obtained through the cattle. A summary is presented below of the positive transfer experiments.

Positive transfer experiments with virus of stomatitis
pustulosa contagiosa equi



Legend: 1) Horse; 2) calf; 3) rabbit; 4) chicken; 5) sheep;
6) rabbit, cutaneous; 7) rabbit, corneal; 8) dog;
9) hog; 10) human.



Fig. 5. Fox in sheep after vaccination
with stomatitis virus after passage
through a calf. Vaccinated on 2 April
1924; picture taken on 7 April 1924

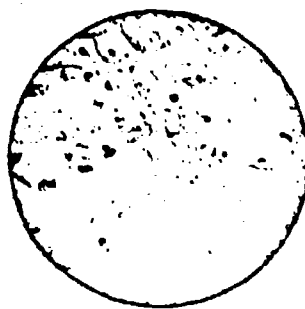


Fig. 6. Guarneri particles in the
cornea of the rabbit, three days
after vaccination with stomatitis
virus after passage through a calf.
Vaccinated on 4 April 1924; enu-
cleation on 7 April 1924; picture
taken on 14 April 1924.

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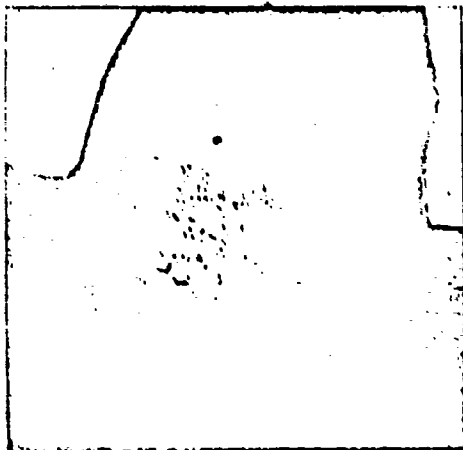


Fig. 7. Pox in the dog after vaccination with stomatitis virus after passage through a calf. Vaccinated on 19 April 1924; picture taken on 17 April 1924.



Fig. 8. Pox in a chicken after vaccination with vaccine. Vaccinated on 26 July 1924; picture taken on 2 August 1924.

The vaccination of the sheep, the dog, and the chicken was performed on the skin in the ventral stomach area after first scarifying the skin.

In the rabbit, vaccination was performed at the depilated skin on the back; in the human, at the depilated skin of the arm; and in the chicken, at the crest and the throat flap. Pronounced poxes developed in all of these animals within 4-6 days. They developed especially clearly in the dog, the rabbit, and the chicken. In the human (I have vaccinated myself) the typical pox did not develop. In this particular instance, this was the result of several prior vaccinations against pox. There was a reaction, however, of the type usually seen in revaccinations, characterized by an accelerated area formation.

The task now was to verify the pox nature of the artificially created efflorescences. This was accomplished by supravaccination of the stomatitis vaccine virus on the corner of a rabbit for identification of Guarnieri particles. As it is well known, the Guarnieri particles are bodily manifestations that occur as cell-reaction products -- according to present interpretation -- in the epithelial cells of the pox-virus vaccinated cornea of the rabbit. These particles are considered as specific for pox. They were indeed identified and thus the pox-nature of the stomatitis virus was verified.

The evidence that the stomatitis virus has a non-lytic nature was further reinforced by subsequent revaccination of the experimental animals that were previously vaccinated with stomatitis virus, to establish whether these animals are immune against vaccine. (cf. the summarizing table of the immunization experiments.) The immunity test was conducted approximately 14 days after the first vaccination in the calves vaccinated with stomatitis material. In the course of these experiments, an early reaction as described by v. Pirquet occurred, same as usually occurs if revaccination closely follows primary vaccination, i.e., only three small pustules developed and then disappeared two days later. In this connection, it should be mentioned that the vaccine employed in the after-vaccination was fully virulent, as shown by control tests on rabbits. The result of the immunity examination agrees with that reported by van Heelsbergen, who was able to show that a calf that had been vaccinated with stomatitis virus has a considerable degree of immunity against the vaccine virus.

In the other animals prevaccinated with stomatitis material, where the vaccination result was positive, the immunity test was performed only 2 and 4 months after the previous vaccination. All animals, except the dog, failed to react to this vaccination. Even in the dog there were only six very small pustules. According to these experiments, therefore, the stomatitis virus exhibited a clear immunisatory effect against the vaccine. The following table provides a view of the immunization tests.

Immunization tests

Experimental animals	Vaccination with stomatitis material	Aftervaccination with vaccine
	Result	Result
Calf	24 March 1924 +	5 April 1924, early react.
Horse	24 March 1924 +	25 July 1924 -
Rabbit No. 1	4 April 1924 +	22 May 1924 -
Rabbit No. 2	4 April 1924 +	22 May 1924 -
Chicken	2 April 1924 +	8 May 1924 -
Sheep	2 April 1924 +	26 July 1924 -
Rabbit No. 3	31 March 1924 +	22 May 1924 -
Rabbit No. 4	31 March 1924 +	22 May 1924 -
Dog	10 April 1924 +	26 July 1924 +
Hog	14 April 1924 +	26 July 1924 -

The test results reported are parallel with those given by de Jong, van Heelsbergen, and partly also with those given by Toth. They show

- 1) that stomatitis pustulosa contagiosa in the horse is to be considered as a pox;
- 2) that there is a close relation between this disease and cattle pox, and, furthermore, when we consider also the results of Gins and Toyoda, there is a close relation between the pox of the various domestic animals and that of the human.

Then, specifically, is the relation between the pox of domestic animals and that of poultry? Are poultry pox and thus also poultry diphteria the same as pox in human and domestic animals? Such relations were until very recently denied. As I have mentioned already, I was able to transfer the stomatitis virus to chickens, same as was before by van Heelsbergen and Toth. Both these researchers and I were successful in transferring the vaccine to poultry. Van Heelsbergen has, subsequently, created stomatitis in humans with the virus of poultry pox, and the stomatitis was the same as the natural variant. I have tried repeatedly to reproduce these results; however, I achieved no success. It should be noted, however, that the positive test results of van Heelsbergen are proofs, whereas my negative test results are not. My repeated attempts to supravaccinate the poultry pox onto the skin of the rabbit and then to the corneal tissue of the rabbit, to be able to identify the Guarnieri particles, were also unsuccessful.* In addition, the tests of van Heelsbergen and Toth, aimed to immunize against poultry pox with stomatitis virus, were also unsuccessful. Whereas, however, van Heelsbergen is nonetheless inclined to see relations between poultry pox and poultry diphteria on the one hand and cattle pox on the other hand -- especially since he was able to provide reasonably high immunity against poultry pox virus with the vaccine virus, -- Toth believes that cattle and poultry pox are two etiologically entirely different diseases since they do not mutually confer immunity. Thus, there exists a gap between the two views. My additional tests to effect clarification did not so far flourish sufficiently to permit me to form a clear opinion for settling this divergence of views. On the other hand, Toyoda succeeded at the laboratory of Gins to transgrow the poultry pox virus through the chicken, the rabbit, and the guinea pig onto humans and sheep. He finds that poultry pox is transferable to rabbits and guinea pigs, with the same histological changes taking place in the process as after vaccination with cattle pox. It should be noted, however, that Toyoda could attain only an incomplete degree of immunity against poultry pox with vaccinated sheep pox lymphes and vaccine; on the other hand, he was able to attain complete immunity with the poultry pox virus through passage in rabbits both in a child and a chicken. Immunity could be also attained in the human and in sheep by pretreatment with cattle pox lymphes against poultry pox.

If one desires to summarize the results of all recent tests on the relation between the various pox types, it may be concluded that there are indeed close relations between these, that the pox varieties of the various domestic animals, including poultry pox and diphteria, are nothing else than local varieties of a pox virus that probably originated from the human.

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* Note made while correcting the Galley: In a subsequently attempted trial it became possible to effect transfer of poultry diptheria onto the cornea of the rabbit, and to identify the Guarnieri particles.